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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/373,182 | 08/12/1999 | KIM MCCLURE | PC10240A | 2284 |
| 23913 | 7590 | 11/17/2004 | EXAMINER | |
| PFIZER INC 150 EAST 42ND STREET 5TH FLOOR - STOP 49 NEW YORK, NY 10017-5612 | | | HANLEY, SUSAN MARIE | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1651 | |

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/373,182 | MCCLURE ET AL. | |
| | Examiner | Art Unit | |
| | Susan Hanley | 1651 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 61 and 81-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 61 and 81-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>8/26/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Susan Hanley is now the examiner for this application. Her contact information appears at the end of this Office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 8/26/04 has been entered.

Claim Rejections - 35 USC § 112

Claims 61 and claims 81-83 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds disclosed in Table A which exhibit 100-fold or 500-fold selectivity for TACE over MMPI, does not reasonably provide enablement for any other compounds having the claimed hydroxamate structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

The claims are drawn to compounds comprising a hydroxamate-substituted ring which have a specific degree of selectivity, 100-fold or 500-fold, for TACE over MMPI. The specification at Table A provides evidence for specific compounds which can meet these claims. However, the claimed generic structure encompasses many more compounds with a variety of structural variations that may or may

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not meet the claimed degree of selectivity. The specification does not provide the skilled artisan with the ability to pick with a reasonable degree of predictability which compounds in broadly claimed genus is encompassed by the functional limitations of the claims regarding the ability of the compound to exhibit the claimed selectivity.

As noted, the specification teaches eight species in Table A that function as selective inhibitors as claimed. However, the specification does not teach how the skilled artisan would choose which species of the genus could selectively inhibit TACE over MMP-1. While the specification teaches how to measure the inhibitory activities of compounds that meet the claimed generic structure, there is no disclosure as to what features of the generic structure would lead the ordinary artisan to choose species with the desired function of selective inhibition of TACE without undue experimentation.

In re Wands stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Besides presenting IC₅₀ values for eight species and teaching how to measure TACE and MMP-1 activities, the specification does not provide any discussion as to the structural elements necessary for a specie of the generic structure to have the desired function: the selective inhibition of TACE compared to MMP-1. The specification also fails to teach the quantity of necessary experimentation for the skilled artisan to practice the claimed invention, especially in light of the lack of teaching of the necessary structural elements to achieve the desired selective enzymatic inhibition. This suggests that there is a high degree of unpredictability in the selection of suitable inhibitors.

As discussed in the Office action of July 11, 2001, there is a lack of references in the prior art that teach actual measured values for the inhibition of TACE and MMP-1 by potential selective inhibitors. Further, the prior art discloses that it takes a great deal of skill on the part of the practitioner to decide

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with some degree of predictability which compounds will have the desired activity. In the review by Beckett et al. (Expert Opinion Ther. Patents, 1998), inhibition of MMP's has long been a therapeutic target and has required joint investigations in the areas of Pharmacology, Medicinal Chemistry, X-ray crystallography and Enzymology. For example, investigators have probed enzyme structure to deduce the structural requirements of active and binding sites. Beckett et al. also teach that many investigators in this area of research utilize Structure Activity Relationships (SAR) studies in an attempt to guide their decision-making process in deciding what species might be a successful inhibitor. The instant specification provides no guidance in any of these areas to lessen the high degree of predictability for choosing a suitable species to serve as a selective TACE inhibitor. Further, there is no functionally and structurally analogous inhibitors which have been identified in the prior art for which this information is known and could be extrapolated to the instant inhibitors by analogy.

While the specification provides assays to determine the inhibitory activities of potential selective inhibitors according to the claimed structure, *In re Wands* determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to specific inhibitors and the instant specification does not provide a description of a repeatable process of producing a selective inhibitor. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination the structural elements which are required for the claimed selectivity. It is this additional characterization of the properties that is required in order to obtain the functional and structural data needed to permit one to produce an inhibitor which meets both the functional requirements of the instant claims that constitutes undue experimentation.

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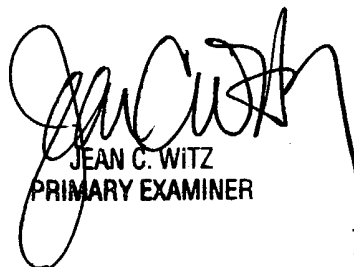
In conclusion, the instant claims encompass a vast, almost limitless, number of inhibitors and yet the instant specification provides limited specific working examples and no general guidance that would permit and artisan to practice the invention commensurate with the scope of the instant claims.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


JEAN C. WITZ
PRIMARY EXAMINER